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## Clinical paper

# Design and implementation of the AIRWAYS-2 trial: A multi-centre cluster randomised controlled trial of the clinical and cost effectiveness of the i-gel supraglottic airway device versus tracheal intubation in the initial airway management of out of hospital cardiac arrest<sup>☆</sup>



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## ABSTRACT

Health outcomes after out of hospital cardiac arrest (OHCA) are extremely poor, with only 7–9% of patients in the United Kingdom (UK) surviving to hospital discharge. Currently emergency medical services (EMS) use either tracheal intubation or newer supraglottic airway devices (SGAs) to provide advanced airway management during OHCA. Equipose between the two techniques has led to calls for a well-designed randomised controlled trial.

The primary objective of the AIRWAYS-2 trial is to assess whether the clinical effectiveness of the i-gel, a second-generation SGA, is superior to tracheal intubation in the initial airway management of OHCA patients in the UK. Paramedics recruited to the AIRWAYS-2 trial are randomised to use either tracheal intubation or i-gel as their first advanced airway intervention. Adults who have had a non-traumatic OHCA and are attended by an AIRWAYS-2 paramedic are retrospectively assessed against eligibility criteria for inclusion.

The primary outcome is the modified Rankin Scale score at hospital discharge. Secondary objectives are to: (i) estimate differences between groups in outcome measures relating to airway management, hospital stay and recovery at 3 and 6 months; (ii) estimate the cost effectiveness of the i-gel compared to tracheal intubation. Because OHCA patient needs immediate treatment there are several unusual features and challenges to the design and implementation of this trial; these include level of randomisation, the automatic enrolment model, enrolment of patients that lack capacity and minimisation of bias.

**Abbreviations:** CAD, computer aided dispatch; CAG, Confidentiality Advisory Group; CPR, cardiopulmonary resuscitation; CRF, case report form; CTEU, Clinical Trials and Evaluation Unit; EAST, East of England Ambulance Service NHS Trust; EMAS, East Midlands Ambulance Service NHS Trust; EMS, Emergency Medical Services; HES, Hospital Episode Statistics; ICC, intraclass correlation; ILCOR, International Liaison Committee on Resuscitation; JRCALC, Joint Royal Colleges Ambulance Liaison Committee; mRS, modified Rankin Scale; NICE, National Institute for Health and Care Excellence; NHS, UK National Health Service; OHCA, out of hospital cardiac arrest; QALY, quality adjusted life year; RCT, randomised controlled trial; ROSC, return of spontaneous circulation; SAE, serious adverse device event; SAE, serious adverse event; SGA, supraglottic airway; SWAST, South Western Ambulance Service NHS Foundation Trust; UK, United Kingdom; YAS, Yorkshire Ambulance Service NHS Trust.

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Patient enrolment began in June 2015. The trial will enrol 9070 patients over two years. The results are expected to influence future resuscitation guidelines.

**Trial Registration** ISRCTN: 08256118.

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## Introduction

The United Kingdom (UK) has the highest reported incidence of out of hospital cardiac arrest (OHCA) in Europe; 123 cases per 100,000 population per annum.<sup>1</sup> Despite recent improvements, survival rates from cardiac arrest remain poor with approximately 7–9% of patients in the UK surviving to hospital discharge, compared with estimates of between 5% and 25% internationally.<sup>2–5</sup> During a cardiac arrest, the brain is exposed to a period of hypoxaemia and ischaemia, which may result in death or cognitive deficits.<sup>6</sup> Optimal cardiopulmonary resuscitation (CPR) and return of spontaneous circulation (ROSC) are key factors associated with avoiding or minimising neurological impairment in the survivors of OHCA,<sup>9,10</sup> and early effective airway management is fundamental to this.

Traditional teaching suggests that tracheal intubation is the best way to manage the airway during OHCA.<sup>11</sup> However, this assumption has not been well tested,<sup>12</sup> and pre-hospital intubation attempts by paramedics can be associated with complications such as interruptions in chest compressions, unrecognised oesophageal intubation (particularly if waveform capnography is not available), and delays in accessing definitive care.<sup>13,14</sup>

Supraglottic airway devices (SGAs) are an alternative to intubation. They are quicker and easier to place and may avoid the complications of tracheal intubation.<sup>15</sup> SGAs are used safely to manage the airway during hospital procedures.<sup>16–18</sup> They are also in widespread use in UK National Health Service (NHS) emergency medical services (EMS); in 2014/15 the London Ambulance Service reported 1469/1775 (83%) successful OHCA intubations, compared to 3149/3494 (90%) successful SGA placements.<sup>5</sup> Equipose between the two techniques has led to recent calls for a large randomised controlled trial (RCT) of the two approaches.<sup>19,20</sup>

Between March 2012 and February 2013 we carried out a study (REVIVE-Airways) in a single NHS EMS provider to assess the feasibility of recruiting paramedics and patients to a study comparing two SGAs (i-gel and the Laryngeal Mask Airway Supreme) with current practice (including tracheal intubation).<sup>21</sup> REVIVE-airways demonstrated that the study was feasible and informed the design of AIRWAYS-2.

The Resuscitation Council (UK) 2015 guidelines state that the optimal airway technique for cardiac arrest is still unknown, and is likely to depend on the skills of the operator, the anticipated pre-hospital time and patient-dependent factors.<sup>22</sup> Evidence-based interventions to improve OHCA survival are still urgently required. The AIRWAYS-2 trial has the potential to answer important questions about initial advanced airway management in OHCA, examining both survival rates and the quality of that survival.

## Methods and analysis

### Aims and objectives

The aim of AIRWAYS-2 is to determine whether the i-gel (Inter-surgical; Wokingham, UK), a second-generation SGA, is superior to tracheal intubation when used by an AIRWAYS-2 study paramedic in non-traumatic OHCA in adults, in terms of both clinical and cost effectiveness.

Specific objectives are to estimate:

1. The difference in the primary outcome of the modified Rankin Scale (mRS) at hospital discharge (or 30 days post OHCA if the patient is still in hospital) between groups of patients managed with either the i-gel or tracheal intubation as their initial advanced airway management strategy following OHCA.
2. Differences in secondary outcome measures relating to airway management, hospital stay and recovery at 3 and 6 months between groups of patients managed with either the i-gel or tracheal intubation.
3. The cost effectiveness of the i-gel compared to tracheal intubation, including estimation of major in-hospital resource use (e.g. length of stay in intensive and high dependency care), and associated costs in each group.

### Design

AIRWAYS-2 is an open parallel two-group multi-centre cluster RCT. The trial schema is shown in Fig. 1. Paramedics rather than patients are randomised to one of the treatment groups and all enrolled patients should be treated according to the enrolling paramedic's allocation.

### Setting

The trial involves collaboration between four UK NHS EMS providers (South Western Ambulance Service NHS Foundation Trust (SWAST), East of England Ambulance Service NHS Trust (EEAST), East Midlands Ambulance Service NHS Trust (EMAS), Yorkshire Ambulance Service NHS Trust (YAS)) and the 95 NHS hospitals served by the participating EMS providers.

### Paramedic population

Paramedics are eligible if they are employed by one of the four participating EMS providers, undertake general operational duties, and can therefore be despatched to attend an OHCA as the first or second paramedic to arrive at the patient's side. They must be registered with the Health and Care Professions Council and be qualified to practice tracheal intubation in their current clinical role.

### Randomisation

In AIRWAYS-2, paramedics working within SWAST, EMAS, EEAST or YAS who consent to participate in the trial are randomly allocated in a 1:1 ratio to one of the two groups: i-gel or intubation (i.e. each paramedic is a randomised cluster).

Randomisation is stratified by EMS provider, years of paramedic experience (greater than or equal to 5 years full-time operational experience versus less than 5 years full-time operational experience) and urban/rural location of the base ambulance station (defined as greater than or equal to 5 miles versus less than 5 miles from the nearest hospital with an emergency department that receives cardiac arrest patients).

Randomisation is performed using a secure computer system developed by the Bristol Clinical Trials and Evaluation Unit (CTEU), with allocation concealment that cannot be changed once allocated.

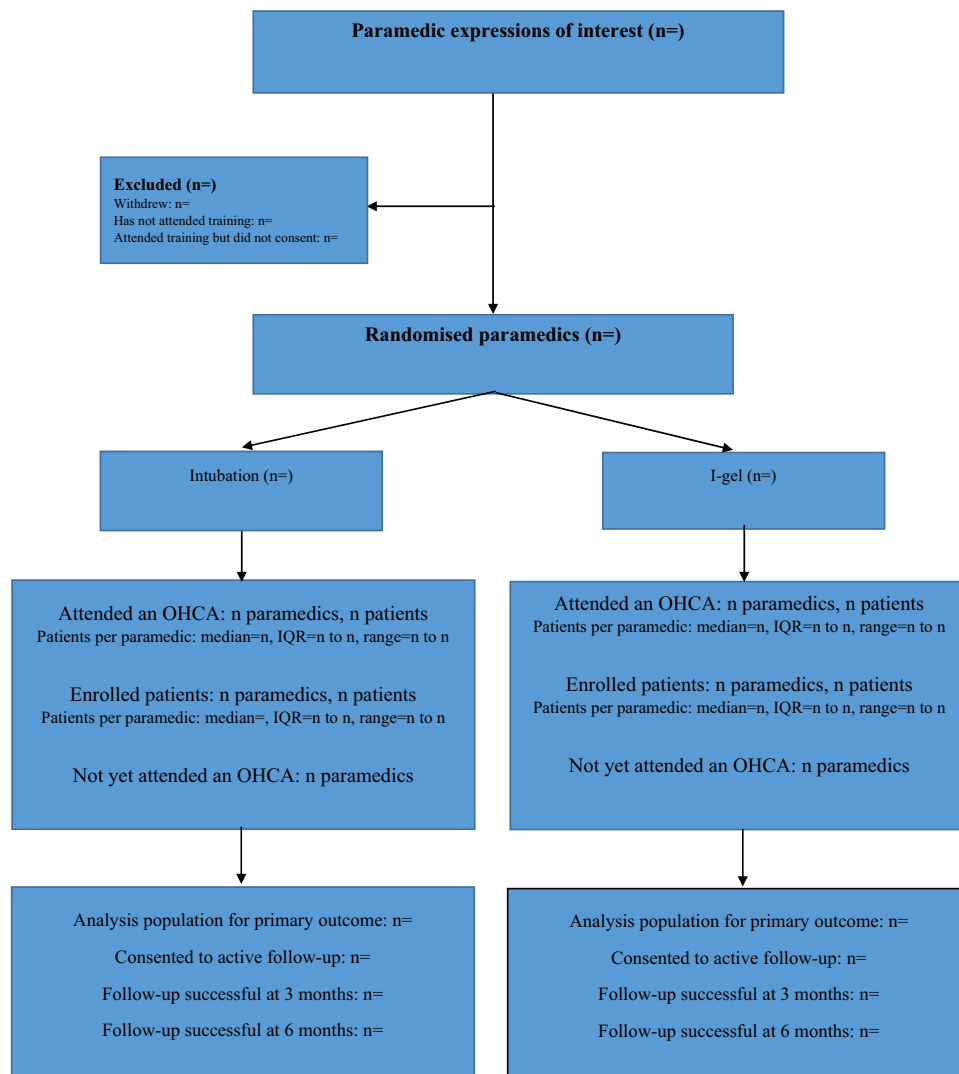


Fig. 1. Consort diagram.

The allocation is not revealed until sufficient information to identify the paramedic has been entered into the system. In order to avoid bias caused by paramedics withdrawing from the study on the basis of their allocation, paramedics are not randomised until half way through a trial specific training session; prior to randomisation the trial design and the need for individual equipoise is explained. If the paramedic is willing to treat all OHCA patient they attend during the study period by either intervention they give consent to take part in the study. The paramedic is then randomised and completes the training session with training that is specific to their allocation.

#### Patient enrolment

Patient inclusion and exclusion criteria are described in Table 1.

In order to prevent paramedics from being able to choose which patients to enrol, this trial uses an automatic enrolment model; all eligible patients attended by an AIRWAYS-2 paramedic for whom resuscitation is attempted are included in the trial. A research paramedic at each ambulance trust then carries out retrospective checks against the study eligibility criteria.

**Table 1**  
Patient inclusion/exclusion criteria.

Inclusion criteria	Exclusion criteria
Patient has had a non-traumatic cardiac arrest outside hospital 18 years of age or older	Patient previously been recruited to the trial (determined retrospectively)
Attended by a paramedic who is participating in the trial and is either the 1st or 2nd paramedic to arrive at the patient's side	Resuscitation is considered inappropriate (based on guidelines produced by the Joint Royal Colleges Ambulance Liaison Committee; JRCALC)
Resuscitation is commenced or continued by EMS staff or responder <sup>a</sup>	Advanced airway management, inserted by another registered paramedic (not participating in AIRWAYS-2) doctor or nurse, is already in place when the AIRWAYS-2 paramedic arrives at patient's side
	They are known to be already enrolled in another pre-hospital RCT
	Mouth opening <2 cm
	Patient detained by Her Majesty's Prison Service

<sup>a</sup> A responder is someone acting for the ambulance service and dispatched by the ambulance service to respond to emergency calls in their local area. They are often a member of the public who is trained by the ambulance service and volunteers.

The automatic enrolment model can give rise to situations which could lead to protocol deviations: (i) ineligible patients may be consciously enrolled (these patients will be excluded from final analysis), (ii) some eligible patients included in the final population may not have been consciously enrolled by the attending AIRWAYS-2 paramedic and (iii) the wrong AIRWAYS-2 paramedic may treat the patient when two or more AIRWAYS-2 paramedics are present on scene.

To ensure near-complete patient identification we are using a triangulation method developed during our feasibility study. Data are collected on all OHCA occurring within each EMS provider from three separate sources:

- A. Direct paramedic report: participating paramedics are asked to complete a case report form (CRF) immediately after each eligible OHCA that they attend, and notify the coordinating research paramedic by telephone, text or e-mail.
- B. Daily review of the EMS computer aided dispatch (CAD) system, by a research paramedic, to identify all 999 calls identified as suspected or confirmed cardiac arrest, and follow-up with the relevant staff to determine whether OHCA had occurred.
- C. Regular review of the OHCA data routinely collected by a participating EMS provider, and reported as part of the Ambulance Service National Quality Indicator set in England.

#### Patient consent

All enrolled patients who survive to hospital admission are followed-up by a member of the research team. If a patient is likely to survive to hospital discharge, the research staff consult with clinical staff caring for the patient to (a) decide whether the survivor has the mental capacity to provide consent, and (b) to determine the optimal time to approach the patient and/or their family to seek consent/assent for further follow-up and data collection.

The patient or consultee can choose one of the following consent options:

- A. Active follow-up: The patient will be actively followed up at discharge, 3 and 6 months after the index OHCA. Quality of life and mRS score will be collected at these time points.
- B. Passive follow-up; routine data will be collected and the patient will not be contacted again about the study.

The patient or consultee can also decline to take part in the study. If this option is chosen no further data collection will take place.

In cases where consultee consent is obtained, patient capacity will be assessed at the 3 and 6 month follow-up. If the patient regains capacity, consent to continue their involvement in the study will be sought from the patient.

#### Trial interventions

##### Tracheal intubation (control group)

The current standard care pathway is tracheal intubation: the placement of a cuffed tube in the patient's trachea to provide oxygen to the lungs and remove carbon dioxide. Tracheal intubation is considered the "gold standard" of airway management, and is used universally in comatose survivors of cardiac arrest following their admission to hospital.

##### i-gel (experimental group)

The intervention being studied is insertion of an i-gel, a second-generation SGA, as an alternative to tracheal intubation.

#### Aspects of airway management common to both groups

A standardised airway management algorithm was developed by the 4 participating EMS providers. Fig. 2a–d focuses on the initial airway management attempts. Full details of the airway management pathway are shown in [Supplementary materials Figs. 1 and 2](#).

Care proceeds as normal for OHCA patients enrolled in the trial, aside from the initial advanced airway management. All other interventions proceed according to standard resuscitation guidelines<sup>22</sup> that are disseminated widely in the UK and internationally. Following ROSC sedation or neuromuscular blockade is not normally provided prior to hospital arrival, and if an airway device is not tolerated it will be removed. Patients who die at the scene are managed in accordance with nationally disseminated EMS protocols. Patients who do not die at scene are transported to hospital and treated using standard post-OHCA care pathways.

Due to the emergency nature of the trial we do expect deviations from the AIRWAYS-2 treatment algorithm. True cross over is defined as the patient receiving the incorrect intervention on the first advanced airway management attempt; other deviations can occur during subsequent airway management attempts (see protocol deviations).

#### Outcome measures

##### Primary outcome

The primary outcome is the modified Rankin Scale (mRS) measured at hospital discharge (or 30 days after OHCA if the patient is still in hospital). The mRS, which incorporates both quality of life and survival, is widely used in OHCA research<sup>25,26</sup> and comprises a seven point scale (0 to 6) with lower scores representing better recovery. Patients who die are given a score of six. The mRS is determined by a research nurse who will assess the patient using a simple flow chart that has been used previously to assess patients who have had a cardiac arrest.<sup>27</sup> With prior permission of the Health Research Authority Confidentiality Advisory Group (CAG), we are collecting survival data and mRS at hospital discharge/30-days for all enrolled patients, regardless of their consent status, thereby ensuring close to 100% ascertainment of the primary outcome.

##### Secondary outcomes

There are 12 secondary outcomes. These are listed in [Table 2](#).

#### Sample size considerations

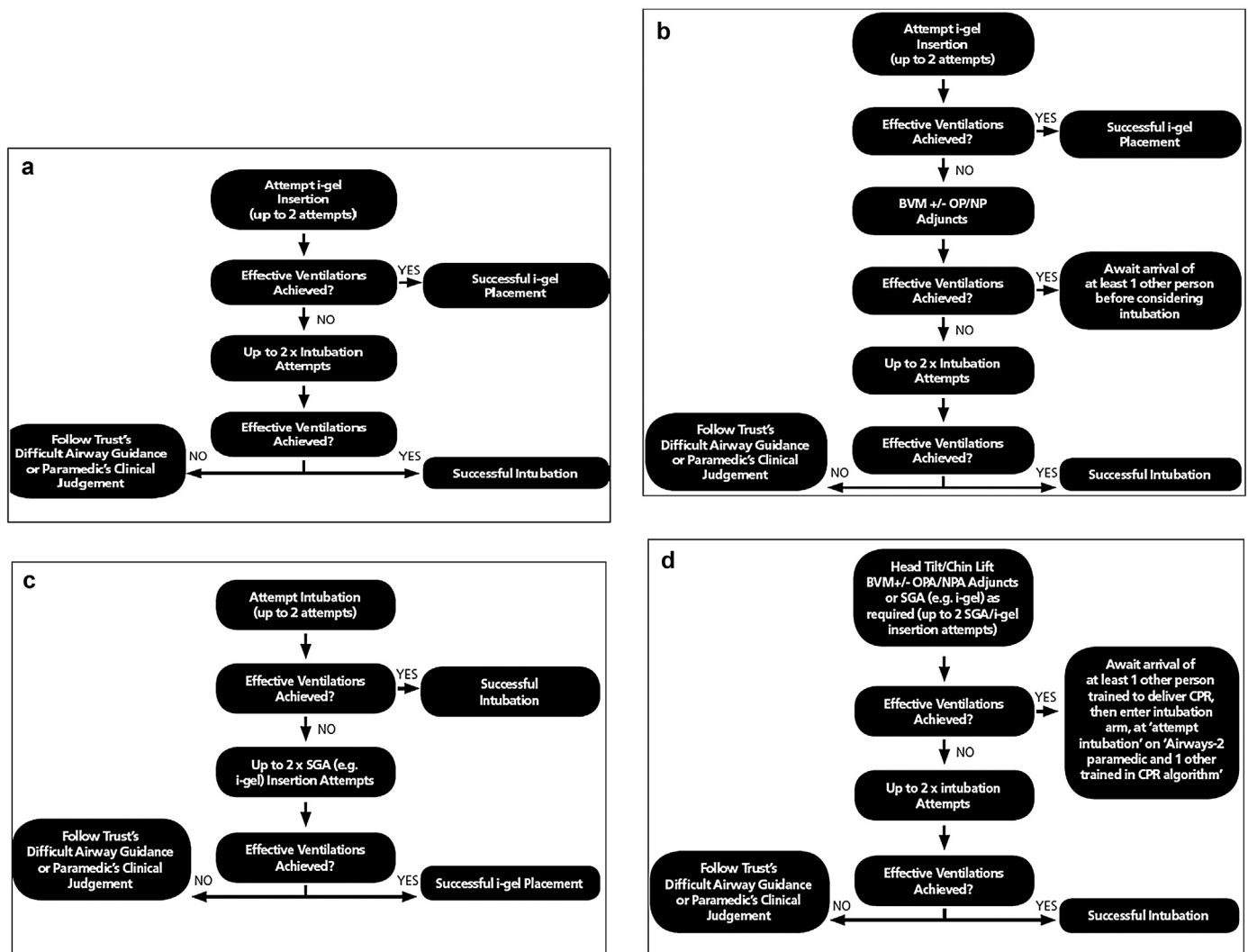
##### Patient sample size

In the REVIVE-Airways feasibility study, 9% of recruited patients survived to hospital discharge.<sup>28,29</sup> This is in-line with the current rate of overall survival to discharge reported by English EMS.<sup>3</sup> Using survival as a proxy for mRS score, a 2% improvement in the proportion of patients achieving a good neurological outcome (defined as an mRS score of 0–3), would be clinically significant, and similar to the 2.4% difference in survival to discharge between tracheal intubation and SGAs reported in a retrospective analysis.<sup>13</sup>

To identify a difference of 2% (8% vs. 10%, i.e. centred on 9%) requires 4400 patients per group (at the 5% level for statistical significance and 90% power). However, each OHCA is not an independent observation, as the patients are nested within a limited number of paramedics participating in the trial. Using data from our feasibility study of 171 paramedics attending 597 OHCA (3.6 patients per paramedic per year), we estimated the intraclass correlation (ICC) to be <0.001. However, when estimating the sample size we have assumed a conservative estimate for the ICC of 0.005. Therefore we require a sample size of 9070 patients (4535 per group).

We powered the trial on mortality rather than mRS because the percentage of patients surviving with a good neurological outcome





**Fig. 2.** Airway management algorithm. (a) i-gel Airways-2 paramedic and at least one other person trained in CPR. (b) i-gel Solo Airways-2 Paramedic Response. (c) Intubation Airways-2 paramedic and at least one other person trained in CPR. (d) Intubation Solo Airways-2 Paramedic Response.

**Table 2**  
Outcome measures and data collection points.

Data item	Out of hospital treatment phase (data collection by paramedics)	In hospital/hospital discharge (data collection by hospital staff)	3 month post OHCA (data collected by research team)	6 month post OHCA (data collected by research team)
<b>Primary and secondary outcomes</b>				
Initial ventilation success (visible chest rise)	✓ <sup>a</sup>			
Regurgitation/aspiration	✓ <sup>a</sup>			
Loss of a previously established airway	✓ <sup>a</sup>			
Actual sequence of airway interventions delivered	✓ <sup>a</sup>			
Return of spontaneous circulation	✓ <sup>a</sup>			
Airway management in place when ROSC achieved or resuscitation discontinued	✓ <sup>a</sup>			
Survival	✓ <sup>a</sup>	✓ <sup>a</sup>	✓ <sup>c</sup>	✓ <sup>c</sup>
Modified Rankin Scale		✓ <sup>a</sup>	✓ <sup>b</sup>	✓ <sup>b</sup>
EQ-5D		✓ <sup>b</sup>	✓ <sup>b</sup>	✓ <sup>b</sup>
Resource use data	✓ <sup>a</sup>	✓ <sup>c</sup>	✓ <sup>c</sup>	✓ <sup>c</sup>
Serious adverse events	✓ <sup>a</sup>	✓ <sup>c</sup>	✓ <sup>c</sup>	✓ <sup>c</sup>
Length of hospital stay (captured separately for different levels of care)		✓ <sup>c</sup>		
<b>Other data items</b>				
Eligibility	✓ <sup>a</sup>			
Demography	✓ <sup>a</sup>	✓ <sup>a</sup>		
Approached for consent		✓ <sup>a</sup>		

<sup>a</sup> Collected for all patients enrolled in trial (where patient survives to that point in the patient pathway).

<sup>b</sup> Only collected for patients that consent to active follow-up.

<sup>c</sup> Only collected for patients that consent to active or passive follow-up.

cannot be greater than the percentage of patients who survive. If we had powered the trial for a 2% difference in mRS, we would not have had 90% power to detect the 2% difference in mortality, which we acknowledge is a key secondary outcome.

#### *Paramedic sample size*

In our feasibility study the mean number of patients enrolled per participating paramedic was 3.6 per year. Therefore in order to enrol the 9070 patients within the two year recruitment period we estimate that we need to recruit at least 1300 paramedics. Across the four EMS providers participating in AIRWAYS-2, there are more than 4300 eligible paramedics; we therefore need to enrol over 30% of the paramedics employed by the four EMS providers.

#### *Paramedic training*

Standardised training materials have been developed to support training in research procedures and the allocated airway management technique for both the intubation and i-gel groups. These are administered to all participating paramedics before enrolment commences, with a research refresher halfway through the recruitment period (at 12 months). Concerns have been raised that after two years using just one method of advanced airway management, participating paramedics risk becoming de-skilled in alternative approaches. Therefore, to support effective paramedic recruitment and retention, we will offer additional exit training to all participating paramedics to update their airway management skills once patient enrolment has been completed.

The AIRWAYS-2 trial has been formally endorsed by the College of Paramedics.

#### *Data collection*

For each eligible OHCA patient enrolled in the trial, the paramedic who enrolls the patient completes an airway management CRF to capture baseline and secondary outcome data. If a patient is admitted to hospital the consent and follow-up process is coordinated by a regionally-based research nurse. Hospitals provide information on patient survival and recovery depending on the consent option chosen by the patient/consultee.

The data collection schedule is summarised in [Table 2](#).

#### *Patient follow-up*

Follow-up occurs at 3 and 6 months ( $\pm 4$  weeks) after OHCA. Patients are asked to complete the level of function survey (mRS-9Q), the EQ5D-5L questionnaire, and a bespoke resource use questionnaire that captures information about (i) any equipment or aids the patient requires, (ii) any stays away from home for medical reasons and (iii) information on any contact with health care professionals. Follow-up is carried out by telephone or post, co-ordinated by the central CTEU team.

#### *Serious adverse event management*

Serious adverse events (SAEs) and serious adverse device events (SADEs) are reported in accordance with the sponsor's research-related adverse event reporting policy.

All trial patients are in an immediately life-threatening situation, most do not survive, and all survivors are hospitalised. SAEs and SADEs are only reported if they are potentially related to trial participation and they are unexpected (i.e. the event is not an expected occurrence for patients who have had a cardiac arrest).

#### *End of the trial*

For patients who consent to follow-up, their participation ends after the final follow-up, six months after the index cardiac arrest. For patients who do not consent to follow-up, their participation ends immediately after approach for consent. The trial will end once all participants have completed the follow-up phase.

#### *Data analysis*

The primary analysis will take place when follow-up is complete for all recruited participants. A formal interim analysis is planned at the mid-point of recruitment. The trial will continue as planned unless the Data Monitoring and Safety Committee recommends termination.

The primary outcome of mRS at discharge or 30 days post OHCA will be dichotomised into good recovery (0–3) versus poor recovery/death (4–6), in line with previous reports. The mRS and other binary outcomes will be analysed using multilevel mixed effects logistic regression models, accounting for the clustering of data within paramedics. Survival to 6 months and other time-to-event outcomes will be analysed using survival analysis methods, again allowing for clustering of patients by paramedic. Overall quality of life utility scores and patient survival will be considered jointly to assess whether the use of the i-gel simultaneously improves the patient's quality of life and reduces the risk of death.

Analyses will be performed according to the principle of intention-to-treat, and reported according to CONSORT guidelines.<sup>30,31</sup> Two sub-group analyses are planned: the Utstein comparator group (defined as an arrest of a presumed cardiac cause that was bystander witnessed with an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia; estimated to make up about 20% of the total) versus non-comparator group, and arrest witnessed by EMS staff (estimated to make up 6% of the total) versus not witnessed by EMS staff.

#### *Protocol deviations*

Most AIRWAYS-2 paramedics attend one to three eligible patients per year and therefore some protocol deviations are expected (see [Supplementary material](#)). To try to reduce deviations as much as possible, monthly monitoring is carried out; research paramedics are required to follow-up protocol deviations with the relevant AIRWAYS-2 paramedic and reiterate the correct procedures. We believe that  $\geq 80\%$  adherence to the AIRWAYS-2 protocol is necessary to maintain the integrity of the study, with  $< 10\%$  "true cross over" (incorrect intervention attempted first).

#### *Economic evaluation*

An economic evaluation is being undertaken as part of AIRWAYS-2 to estimate the cost effectiveness of the i-gel compared to intubation, in accordance with recognised National Institute for Health and Care Excellence (NICE) guidelines.<sup>32</sup> This will help to determine which type of airway management represents the best use of NHS resources in this context.

#### *Planned dissemination*

A strategy has been implemented that includes dissemination of the trial outputs to EMS providers in the UK and overseas, to NHS hospitals and through a publicly accessible website. Findings will be published in high-impact journals, presented at conferences, circulated in newsletters and will also be shared with international groups responsible for the development of resuscitation guidelines.

## Research approvals

Research ethics approval was granted by the Oxford C-South Central Research Ethics Committee (reference 14/SC/1219) in September 2014 and the Confidentiality Advisory Group gave approval for the trial under Regulation 5 of the Health Service (Control of Patient Information) Regulations 2002 to process patient identifiable information without consent.

## Trial management

The Sponsor organisation is the South Western Ambulance Services NHS Foundation Trust.

The contribution of the manufacturers of the i-gel is limited to confirming that the training of paramedics in the use of the devices conforms to their recommended guidelines. The manufacturer has no role in supplying devices or the design, conduct, analysis or reporting of the trial.

The trial is overseen by a Trial Steering Committee and Data Monitoring and Safety Committee.

A patient and public research advisory group consisting of 10 members meets every 4–6 months. The advisory group are involved in debating various challenges regarding patient involvement; their feedback has helped inform the design of the study.

## Discussion

Due to OHCA being an extreme medical emergency requiring immediate attendance and action by skilled clinical staff in a wide range of unpredictable environments, the implementation and design of the AIRWAYS-2 trial has presented several challenges relating to both ethical considerations around patient consent and the potential for bias.

As AIRWAYS-2 involves the recruitment of incapacitated adults and there is no opportunity to obtain informed consent prior to treatment, we use a deferred consent model for survivors and waiver of consent for those who do not survive to discharge from intensive/coronary care. Following consultation with our patient and public advisory group we made the decision not to inform the relatives of enrolled patients who do not survive the initial cardiac arrest that they were involved in research; this applies to the majority of patients enrolled, and is a model that was adopted successfully in our feasibility study. Informing relatives that their recently deceased loved one was involved in research has a high risk of increasing distress and uncertainty without benefit. We believe that this approach represents the best way of answering this important clinical question, and that the trial is justified by both its relevance to future healthcare and the degree of clinical equipoise that currently exists, since both tracheal intubation and the i-gel are already used routinely in English EMS providers, and information on the advanced airway management strategies used during resuscitation is not routinely provided to the relatives of patients who do not survive OHCA.

To minimise bias we are using a combination of methods to identify all eligible patients, and an objective primary outcome measure (mRS) that with the permission of the CAG, can be obtained for all surviving patients regardless of their consent status.

Ideally a trial would randomise at the level of the patient. However, due to the emergency situation this is not practicable in AIRWAYS-2. The procedures that would be required to achieve randomisation of an eligible patient (contacting a remote server or telephone line, or even opening a sealed opaque envelope) are impracticable at the point when an eligible patient is identified. One could argue that it would be possible to randomise at patient level on the way to an arrest but patient level randomisation before patient eligibility is assessed would lead to many ineligible patients

being randomised. Almost all similar research studies have been cluster-randomised, often at the level of ambulance stations,<sup>33–35</sup> which has also led to challenges relating to adherence with the allocated interventions and bias. On the basis of the REVIVE-Airways feasibility study,<sup>28,29</sup> we chose to randomise paramedics, which is advantageous because it more closely approaches individual patient randomisation (i.e. more clusters and fewer participants per cluster).

One of the key challenges faced whilst designing the AIRWAYS-2 study was ensuring that there was a robust model of patient enrolment. The automatic patient enrolment model used in this study has the advantage of ensuring that all eligible patients are identified and included in the study population. This significantly reduces the ability of AIRWAYS-2 paramedics to introduce selection bias.

The use of an automatic enrolment model could however increase the likelihood of protocol deviations, including non-adherence to the airway management algorithm. The automatic enrolment model will also have some limitations that may affect the quality of the data; if a patient is included in the study that the AIRWAYS-2 paramedic did not consciously enrol this may lead to missing airway management data or poor quality data if an AIRWAYS-2 paramedic is asked to retrospectively recall the details of an event.

The results from the AIRWAYS-2 trial, together with results from the PART trial (a similar North American study),<sup>36</sup> have the potential to answer important questions about initial advanced airway management in OHCA. It is hoped that findings from these trials will help to reduce premature mortality, enhance quality of life and reduce the use of health and social care resources by leading to important changes in the treatment protocols recommended by the International Liaison Committee on Resuscitation (ILCOR).

## Trial status

The first paramedic was randomised in March 2015. The trial opened to patient enrolment in three EMS providers in June 2015 and the other EMS provider in July 2015. Paramedic and patient recruitment is on-going.

The full protocol is available from [www.nets.nihr.ac.uk/projects/hta/12167102](http://www.nets.nihr.ac.uk/projects/hta/12167102).

## Independent Trial Steering Committee members

- Simon Gates (Chair), Professor of Clinical Trials, University of Warwick.
- Charles Deakin, Honorary Professor of Resuscitation and Pre-Hospital Emergency Medicine, University of Southampton University of Southampton.
- Gavin Perkins, Clinical Professor in Critical Care Medicine, University of Warwick.
- Jas Soar Consultant in Anaesthesia and Intensive Care medicine, Southmead Hospital.
- Keith Douglas, Lay Member.
- Margaret Douglas, Lay Member.

## Independent data monitoring and safety committee members

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- Helen Snooks, Professor of Health Services Research, Swansea University.
- Tom Quinn, Professor of Nursing, Kingston University London and St George's, University of London. Prof Andy Newton, Chief Clinical Officer, South East Coast Ambulance Service NHS Foundation Trust.



## Conflict of interest statement

The authors declare no financial or other conflicting interests.

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## Authors' contributions

All authors contributed to the trial protocol. JRB, CAR, BCR led the application for funding. ES and SW designed the health economic evaluation. JT and JRB drafted the manuscript, all authors contributed to its critical review and read and approved the final version.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.resuscitation.2016.09.016>.

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